Modeling of Tumor Growth and its Control via Paclitaxel Using a Delay Differential Equation

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Paclitaxel is shown to be antiangiogenic at low doses, but the extent of these effects is not known. Our research considers a mathematical model that describes tumor growth and response to treatment with a continuous, low dose treatment of the anti-mitotic drug Paclitaxel. We constructed a model with three populations: system cells, proliferating tumor cells, and tumor cells in a resting phase. A delay differential equation model accounts for the time it takes for tumor cells to complete one cycle in the proliferation phase. We analyzed the system without drug administration, and then ran numerical simulations under different levels of drug administration. We also performed sensitivity analysis on certain parameters to determine what the likely consequences of antiangiogenic effects.

Studies have suggested that well-tolerated chemotherapy can exert a better antitumor effect than conventional high-dose, temporarily spaced-out chemotherapy(2). Moreover, at lower doses the anti-mitotic drug Paclitaxel has been shown to have antiangiogenic effects. Since it is very hard to show the exact extent of those effects in clinical testing, we are creating a mathematical model of tumor growth with only the antimitotic effects. We can then do sensitivity analysis to determine the response of the stability of the equilibria to the antiangiogenic effects of Paclitaxel at low doses. Therefore, we consider a model that describes tumor growth with a continuous, low dose treatment of the anti-mitotic drug Paclitaxel.

A delay differential equation model has been used in previous studies to analyze the role of the conventional chemotherapy treatment, and we see the delay necessary in understanding the full dynamics of tumor growth(1). For the delay case we computed the effect of different chemotherapy controls, i.e. different drug rates, on the stability of the equilibria numerically.

In the non-delay case we computed the effect of different chemotherapy regimes on the presence and stability of equilibria. We found that the tumor free equilibrium was stable only when the drug was present and was at a level higher than the mitosis rate. The tumor free equilibrium was present and stable only under possibly a narrow range of certain conditions, presented above. Sensitivity analysis suggested that the most plausible effects of antiangiogenesis had no effect on the presence or stability of the tumor free equilibrium. However, because we know antiangiogenic drugs effectively reduce tumor growth, our findings suggest that they might reduce the rate of cells leaving the mitotic phase via mitosis.

Simulations showed that continual administration of drugs is preferable to pulsed administration, even when it consists of long pulses with short periods without the drug. This finding is expected because in the absence of chemotherapy the tumor grows at an exponential rate, which can quickly eliminate any benefits of chemotherapy. This finding has been supported by clinical research, where shorter periods between doses of chemotherapy have been shown to be more effective than the standard three weeks.

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